REMARKS

I. Status of the Claims

The claims are 22-48. Claims 1-4, 14 and 15 have been canceled and new claims 22-48 have been added. For the convenience of the Examiner, a copy of the pending claims are included as **Exhibit A**.

II. Support for the Claims

Support for newly added claims 22-48 can be found in the specification as originally filed. More particularly, at page 8, line 6, the term Pablo is defined as a "pro-apoptotic Bcl-xL binding protein." Support for claims 22-25, wherein a Pablo protein modulates apoptosis, can be found at least at page 7, lines 26-30, and in Examples 2-4, page 94, line 12 through page 97, line 21. Support for modulating apoptosis in a neural cell can be found at least at page 3, lines 16-17. Support for claims 26 and 27 can be found at least at page 5, lines 14-16. Support for claims 28-32 can be found at page 53, line 20 through page 57, line 6. Support for claims 33-35 and 37 can be found at page 47, line 9 through page 53, line 19 and page 64, line 28 through page 74, line 9. Support for claim 36 can be found at page 74, line 10 through page 75, line 10. Support for claims 38-40 and 45-48 can be found at page 54, line 9 through page 57, line 6. Support for claims 41and 42 can be found at 24, line 23 through page 26, line 24 and at page 62, line 26 through page 92, line 23. Support for claims 43 and 44 can be found at page 47, line 9 through page 53, line 12.

III. Response to the Objection to the Specification

The Examiner objects to the specification because it contains an embedded hyperlink and/or other form of browser executable code. Applicants have amended the specification, at

page 31, lines 14-15, page 32, line 30, page 96, lines 1-2 and page 96, lines 8-9, to conform with M.P.E.P. § 608.01.

IV. Response to Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 1 and 2 have been canceled, therefore the Applicants respectfully request withdrawal of the rejection of claims 1 and 2 under 35 U.S.C. § 112, first paragraph, as mute.

V. Response to Rejection Under 35 U.S.C. § 102

Claims 1-4, 14 and 15 have been canceled, therefore the Applicants respectfully request withdrawal of the rejection of claims 1-4, 14 and 15 under 35 U.S.C. § 102(b).

VI. Conclusion

It is the Applicants belief that claims 22-48 are in condition for allowance, and action towards that effect is respectfully requested. If there are any matters which may be resolved or clarified through a telephone interview, the Examiner is requested to contact the undersigned attorney at the number indicated.

Respectfully submitted,

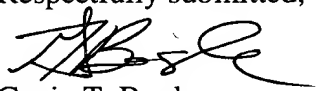

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Exhibit A

Claims Pending in AM100012

22. A method for modulating apoptosis in a cell comprising modulating the activity of a Pablo polypeptide.

23. The method of claim 22, wherein the cell is a neural cell.

24. A method for modulating apoptosis in a cell comprising modulating the expression of a polynucleotide encoding a Pablo polypeptide.

25. The method of claim 24, wherein the cell is a neural cell.

26. A method for treating a subject for a nervous system disorder comprising modulating the activity of a Pablo polypeptide.

27. A method for treating a subject for a nervous system disorder comprising modulating the expression of a polynucleotide encoding a Pablo polypeptide.

28. A method for assaying the effects of test compounds on the activity of a Pablo polypeptide comprising the steps of:
    (a) providing a transgenic animal comprising a polynucleotide encoding a Pablo polypeptide;
    (b) administering a test compound to the animal; and
    (c) determining the effects of the test compound on the activity of the Pablo in the presence and absence of the test compound.

29. The method of claim 28, wherein the polynucleotide has at least one mutation selected from the group consisting of nucleotide deletion, nucleotide substitution and nucleotide insertion.

30. A method for assaying the effects of test compounds on a transgenic animal with a genome comprising a functional disruption of a polynucleotide encoding a Pablo polypeptide, the method comprising:

(a) providing a transgenic animal whose genome comprises a disruption of an endogenous polynucleotide encoding a Pablo polypeptide;

(b) administering a test compound to the animal; and

(c) determining the effects of the test compound on the activity of the Pablo polypeptide in the presence and absence of the test compound.

31. The method of claim 30, wherein the animal is heterozygous for the functional disruption of the endogenous polynucleotide.

32. The method of claim 30, wherein the animal is homozygous for the functional disruption of the endogenous polynucleotide.

33. A method for assaying the effects of test compounds on the activity of a Pablo polypeptide comprising the steps of:

(a) providing recombinant cells comprising a polynucleotide expressing a Pablo polypeptide;

(b) contacting the cells with a test compound; and

(c) determining the effects of the test compound on the activity of the Pablo in the presence and absence of the test compound.

34. The method of claim 33, wherein the polynucleotide has at least one mutation selected from the group consisting of nucleotide deletion, nucleotide substitution and nucleotide insertion.

35. The method of claim 33, wherein the recombinant cell further comprises a polynucleotide expressing a Bcl-xL polypeptide.

36. A method for assaying the effects of test compounds on the binding interaction of Bcl-xL and Pablo polypeptides comprising the steps of:

(a) providing yeast cells for a yeast two-hybrid system comprising a Bcl-xL polypeptide and a Pablo polypeptide;

(b) contacting the cells with a test compound; and

(c) determining the effect of the test compound on the binding interaction of the Bcl-xL and Pablo polypeptides in the presence and absence of the test compound.

37. A method of producing a Pablo polypeptide:

(a) transfecting, transforming or infecting a recombinant host cell with an expression vector comprising a polynucleotide comprising a nucleotide sequence of SEQ ID NO:1;

(b) culturing the host cell under conditions sufficient for the production of the polypeptide; and

(c) isolating the polypeptide from the culture.

38. A method for producing a transgenic animal whose genome comprises a functional disruption in a polynucleotide encoding a Pablo polypeptide, the method comprising:

(a) providing a polynucleotide encoding a Pablo polypeptide having a functional disruption;

(b) introducing the disrupted polynucleotide into embryonic stem cells;

(c) selecting those embryonic stem cells that comprise the disrupted polynucleotide;

(d) introducing an embryonic stem cell of step (c) into a blastocyst;
transferring the blastocyst of step (d) to a pseudopregnant animal; and

(e) allowing the transferred blastocyst to develop into an animal chimeric for the disruption.

39. The method of claim 38, further comprising breeding the chimeric animal with a wild-type animal to obtain animals heterozygous for the disruption.

40. The method of claim 39, further comprising breeding the heterozygous animal to generate animal homozygous for the disruption.

41. A method for the treatment of a subject in need of reduced Pablo activity comprising:

(a) administering to the subject a therapeutically effective amount of a Pablo antagonist; and/or

(b) administering to the subject a polynucleotide encoding an antisense RNA polynucleotide comprising a nucleotide sequence that is a complement to a nucleotide sequence of SEQ ID NO:1 or a fragment thereof.

42. A method for the diagnosis of a disease or the susceptibility to a disease in a subject related to the expression or activity of a Pablo polypeptide in the subject comprising:

(a) determining the presence or absence of a mutation in a polynucleotide encoding a Pablo polypeptide comprising an amino acid sequence of SEQ ID NO:2 or a fragment thereof; and/or

(b) assaying for the presence of Pablo expression in a sample derived from the subject, wherein the Pablo expressed is a polynucleotide encoding a Pablo polypeptide comprising an amino acid sequence of SEQ ID NO:2 or a fragment thereof.

43. A recombinant expression vector comprising a polynucleotide encoding a Pablo polypeptide comprising the amino acid sequence of SEQ ID NO:2.

44. A genetically engineered host cell, transfected, transformed or infected with the vector of claim 43.

45. A transgenic animal comprising a polynucleotide encoding a Pablo polypeptide comprising an amino acid sequence of SEQ ID NO:2.

46. The transgenic animal of claim 45, wherein the polynucleotide comprises a mutation which modulates Pablo activity.

47. The transgenic animal of claim 49, wherein the animal is heterozygous for the mutation.

48. The transgenic animal of claim 49, wherein the animal is homozygous for the mutation.

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UNITED STATE PATENT AND TRADEMARK OFFICE

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Expires: July 8, 2002

Harry I. Moatz
Director of Enrollment and Discipline